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# Race-ethnicity is related to biomarkers of iron and iodine status after adjusting for sociodemographic and lifestyle variables in NHANES 2003-20061,,2,,3

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#### Abstract

The NHANES 2003-2006 has assessed iron and iodine status, 2 trace element nutrients of continued public health interest, in the US population. We investigated associations of sociodemographic (age, sex, race-ethnicity, education, income) and lifestyle variables (smoking, alcohol consumption, BMI, physical activity, dietary supplement use) with iron status indicators (serum ferritin, soluble transferrin receptor [sTfR], and body iron) in women 20–49 y (n = 2539, 2513, 2509, respectively) and with urine iodine, a biomarker of iodine intake, in adults 20 y (n =3066). Significant correlations between the study variables and biomarkers were weak (|r| 0.24). Urine creatinine (uCr) was moderately significantly correlated with urine iodine (r = 0.52). The individual variables explained 5% of the variability in biomarker concentrations in bivariate analysis. In multiple regression models, sociodemographic and lifestyle variables together explained 4%-13% of the variability of iron indicators and 41% of the variability of urine iodine (uCr in the model). The adjusted estimated body iron was ~1 unit (mg/kg) lower in non-Hispanic black vs. non-Hispanic white women, and ~1 unit higher in women who smoked vs. those who did not, and in women consuming 1 vs. 0 alcoholic drinks/d. The adjusted estimated urine iodine concentration (uCr in the model) was 34% lower in non-Hispanic blacks vs. non-Hispanic whites, 22% higher in supplement users vs. nonusers, and 11% higher with every 10 y increase in age. In summary, after adjusting for sociodemographic and lifestyle variables (and uCr in the iodine model), race-ethnicity retained a strong association with sTfR, body iron, and urine iodine; smoking and alcohol consumption with iron biomarkers; and supplement use and age with urine iodine.

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<sup>&</sup>lt;sup>3</sup>Supplemental Tables 1–4 and Supplemental Figures 1–2 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.

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<sup>&</sup>lt;sup>4</sup>Abbreviations used: FER, serum ferritin; MA, Mexican American; NCHS, National Center for Health Statistics; NHB, non-Hispanic black; NHW, non-Hispanic white; PIR, poverty income ratio; sTfR, soluble transferrin receptor; uCr, urine creatinine.

# INTRODUCTION

Iron and iodine are 2 important trace element nutrients required for health and development. Iron deficiency is linked to adverse consequences, such as reduced physical capacity, poor pregnancy outcomes, and negative effects on cognitive development among infants and adolescents. The reduction of iron deficiency in children and women of childbearing age, 2 at-risk groups, is of continued public health interest and included among the objectives for Healthy People 2020 (1). Monitoring the iron status of the US population has been an important component since the inception of NHANES in 1971, and each survey has included a battery of hematologic and biochemical indicators (up to 2010) of iron status (2). In 2003, the measurement of serum soluble transferrin receptor (sTfR)<sup>5</sup> was introduced, which allows the evaluation of iron status by the body iron model developed by Cook et al. (3). Body iron, estimated from the ratio of sTfR to serum ferritin (FER), assesses the full range of iron status of populations and is in positive balance (0 mg/kg) when there is residual storage iron or in negative balance (<0 mg/kg) when there is functional iron deficiency. The body iron methodology is also less affected by inflammation than the previously used ferritin model (4), which defined iron deficiency as having 2 abnormal out of 3 indicators (FER, transferrin saturation, and erythrocyte protoporphyrin). Different studies have assessed how iron status biomarkers in NHANES may be related to demographic and socioeconomic variables (5–9), dietary intake (10), and supplement use (11).

Iodine is required by the thyroid gland to produce thyroid hormones necessary for normal growth and brain development (12). The most critical period of iodine sufficiency is in utero through the first 2 y of life (13). It has been reported that subgroups of reproductive age women in the United States may be at risk for iodine deficiency (14). The WHO has defined nutritional iodine sufficiency for a population by the median urine iodine concentration (13). A biomarker of iodine intake, urine iodine has been used to monitor the iodine status of the US population in the NHANES since 1971 (15–18). However, little information is available from NHANES on the association of urine iodine concentrations with socioeconomic (14) and selected lifestyle variables such as supplement use (19), smoking (20), and salt consumption (21).

The CDC's Second National Report on Biochemical Indicators of Diet and Nutrition in the US Population (Second Nutrition Report) used data from NHANES 2003–2006 to provide a descriptive analysis of the nutritional status of Americans by age, sex, and race-ethnicity (22). These analyses however, provide only limited interpretation of relative differences in nutritional status by demographic subgroup. As an extension of the Second Nutrition Report and in order to examine whether demographic differentials in nutritional status found in the Second Nutrition Report were related to and confounded by certain variables, we conducted an analysis to examine the association between key sociodemographic (age, sex, race-ethnicity, education, and income) and lifestyle variables (supplement use, smoking, alcohol consumption, BMI, and physical activity) with biomarkers of iron (women 20–49 y) and iodine (men and women 20 y) status in US adults participating in NHANES 2003–2006. The results derived from our descriptive regression model may serve as a foundation to researchers who develop predictive regression models for specific hypotheses on nutrition and health using data from NHANES. Because iron and iodine both belong to the class of

trace elements, they are presented together in the *Second Nutrition Report* as well as in this publication. Companion publications in this journal supplement address the same questions for the other nutrient classes featured in the *Second Nutrition Report*.

## **SUBJECTS AND METHODS**

The NHANES collects cross-sectional data on the health and nutritional status of the civilian non-institutionalized US population (23). The survey obtains a stratified, multistage, probability sample designed to represent the US population on the basis of age, sex, and race-ethnicity. All respondents gave their informed consent, and the NHANES protocol was approved by the NCHS Research Ethics Review Board. Details on what information is collected in NHANES are presented elsewhere (24).

## Laboratory methods

The following iron and iodine status biomarkers were analyzed by the CDC laboratory during NHANES 2003–2006: FER, sTfR, body iron (calculated), and urine iodine. Information for each biomarker on the specimen matrix, the NHANES survey period and population assessed, the laboratory method used, and how we calculated body iron for this analysis is presented in Supplemental Table 1. Additional laboratory method details are provided elsewhere (25,26). Westgard-type QC multi-rules were used to judge assay performance (27).

### Study variables

For bivariate analyses, we categorized the variables as follows: age (20–39 y, 40–59 y, and 60 y for urine iodine; 20–39 y and 40–49 y for iron biomarkers); sex (men and women for urine iodine; women for iron biomarkers); race-ethnicity (Mexican American [MA], non-Hispanic black [NHB], and non-Hispanic white [NHW]); education (<high school, high school, and >high school); family poverty income ratio (PIR: 0–1.85 [low], >1.85–3.5 [medium], and >3.5 [high]) (28); smoking (serum cotinine 10  $\mu$ g/L [nonsmoker], >10  $\mu$ g/L [smoker]) (29); alcohol consumption (average daily number of "standard" drinks [1 drink  $\approx$  15 g ethanol]: no drinks, <1 (not 0), 1–<2, and 2 drinks/d); BMI (kg/m²: <18.5 [underweight], 18.5–<25 [normal], 25–<30 [overweight], and 30 [obese]) (30); physical activity (total metabolic equivalent task [MET]-min/wk from leisure time physical activity; none reported, 0–<500, 500–<1000, and 1000 MET-min/wk) (31); supplement use (reported taking a dietary supplement within the past 30 d: yes [user], no [non-user]).

#### **Analytic sample**

All participants examined in the mobile examination center aged 20 y and older in the NHANES 2003–2004 and 2005–2006 with at least 1 biomarker of interest were eligible for inclusion in the study. Depending on whether the biomarker was analyzed on the full sample or a subsample, data were available for ~2500 women (iron biomarkers) and ~3000 men and women (iodine) (Supplemental Table 2). Because we wanted to assess associations in the general US population, we did not exclude participants. Furthermore, considering all the potentially relevant exclusions in an analysis with multiple biomarkers would have been impractical. However, we verified that excluding participants who reported having had a

thyroid problem at some point (~1% of participants) did not substantially alter the geometric mean of urine iodine compared to not excluding them.

#### Statistical methods

As we used the same statistical methods for the series of papers presented in this supplement, the reader is referred to Sternberg et al. (32) for a detailed description of the methods and for a discussion of compromises taken in developing the multiple regression model due to the limited degrees of freedom, such as the number of covariates considered, the chosen form of continuous covariates, and the consideration of interactions between covariates. In short, we assessed bivariate associations between biomarkers and study variables by calculating Spearman correlations and by presenting the geometric means (arithmetic mean for body iron as its distribution was reasonably symmetric) and 95% CI across the variable categories. We used multiple linear regression to assess the impact of confounding and determine whether statistical significance persists after adjusting for differences in key variables. We arranged the independent variables into 2 sets or "chunks": 1) sociodemographic variables (age, sex, race-ethnicity, education level, and PIR) and 2) lifestyle variables (dietary supplement use, smoking, alcohol consumption, BMI, and physical activity level). We tested each chunk simultaneously to determine whether the independent variables (as a group) were related to the dependent variable; followed by a test for each individual variable while controlling for the other variables. We present the results of 3 regression models for each biomarker: simple linear regression (model 1), multiple linear regression model with the sociodemographic chunk (model 2), and multiple linear regression model with both the sociodemographic and lifestyle chunk (model 3). This allows for the comparison of results across all biomarkers. For urine iodine we assessed a fourth model, in which we included urine creatinine (uCr) as a covariate to adjust for the dilution of the spot urine. For each model we present the estimated percent change (absolute unit change for body iron) in biomarker concentrations with change in each covariate holding all other remaining covariates constant. Estimates were not reported if the minimum sample size of 42 was not reached (assumed average design effect of 1.4 multiplied by 30). Twosided *P*-values were flagged as statistically significant if <0.05.

# **RESULTS**

A description of the civilian noninstitutionalized US population by the variables studied using NHANES 2003–2006 can be found in Supplemental Table 3. The continuous variables (age, PIR, smoking, alcohol consumption, BMI, and physical activity) were weakly significantly (|r| 0.24) or not at all significantly correlated with iron and iodine status biomarker concentrations (Table 1). As expected, urine creatinine was moderately significantly correlated with urine iodine (r = 0.52).

Bivariate methods (model 1) were used to test for significant differences among variable categories. Of the sociodemographic variables, only race-ethnicity and PIR had significant associations with FER and sTfR, while all 5 sociodemographic variables were significantly associated with urine iodine (Table 2). Of the lifestyle variables, smoking and alcohol consumption had significant associations with all 3 iron status indicators, while BMI was

significantly associated with sTfR and body iron only (Table 3). Physical activity was not significantly associated with iron status indicators. All 5 lifestyle variables had significant associations with urine iodine except for smoking status. Overall though, these individual variables explained little ( $r^2$  5%) of the variability in biomarker concentrations.

Using multiple regression models, the sociodemographic variables together (model 2) explained up to 6% of the variability in iron status indicators (2% [FER and body iron] and 6% [sTfR]) and 5% for urine iodine (Supplemental Table 4). Together, the sociodemographic and lifestyle variables (model 3) explained up to 13% of the variability in iron status indicators (4% [FER], 5% [body iron], and 13% [sTfR]) and 7% for urine iodine. When we also adjusted for uCr (model 4), 41% of the variability in urine iodine concentrations was explained. Adjusting for sociodemographic and lifestyle variables together generally led to an attenuation of *beta* coefficients (model 3 vs. model 2), suggesting that sociodemographic variables may capture some unmeasured effect that was shared with lifestyle variables. The additional adjustment for uCr in model 4 for urine iodine had different effects on *beta* coefficients depending on the variable: further attenuation for sex, PIR, alcohol consumption, and BMI; increase for age, race-ethnicity (NHB vs. NHW), and supplement use; and no change in the association with race-ethnicity (MA vs. NHW), education, smoking, and physical activity.

Because the log transformations may obscure the interpretation of the beta coefficients, we estimated the percent change in biomarker concentrations (change in mg/kg for body iron which was not log transformed) associated with each covariate. Based on the full regression model 3, only smoking and alcohol consumption were significantly and strongly associated with all 3 iron status indicators (Table 4 and Supplemental Fig. 1). We observed significant associations with only 2 markers for age (FER and body iron), race-ethnicity (NHB vs. NHW; sTfR and body iron), PIR (sTfR and body iron), and BMI (FER and sTfR). Physical activity was significantly associated with FER only; education, supplement use, and raceethnicity (MA vs. NHW) were not significantly associated with either of the iron biomarkers. The estimated change in body iron (model 3) was ~1 unit (mg/kg) lower in NHB vs. NHW women, and ~1 unit higher in women who smoked vs. did not smoke, and in women consuming 1 vs. 0 alcoholic drinks/d. Estimated FER (decreases with poor iron status) and sTfR (increases with poor iron status) concentrations were 7% lower and 19% higher in NHB vs. NHW women, 24% higher and 11% lower in smoking vs. nonsmoking women, and 21% higher and 6% lower in women consuming 1 vs. 0 alcoholic drinks/d, respectively. A 25% increase in BMI was associated with 7% and 6% higher FER and sTfR concentrations, respectively, but no change in body iron. A 10 y increase in age was associated with 8% higher FER concentrations and 0.2 mg/kg higher body iron.

Based on the full regression model 4, only age, race-ethnicity (NHB vs. NHW), supplement use, and alcohol consumption were significantly associated with urine iodine (Table 4 and Supplemental Fig. 2). The estimated urine iodine concentration (model 4) was 34% lower in NHB vs. NHW, 22% higher in supplement users vs. nonusers, 11% higher with every 10 y increase in age, and 7% lower in adults consuming 1 vs. 0 alcoholic drinks/d. Women had lower estimated urine iodine concentrations (~20%) compared to men for models 1–3,

however when we also adjusted for urine creatinine in model 4, the sex difference disappeared.

## DISCUSSION

This analysis of iron and iodine status biomarkers in a nationally representative sample of American women (iron) and adults (iodine) participating in NHANES 2003–2006 showed the following after adjusting for key sociodemographic and lifestyle variables (and uCr for urine iodine): 1) race-ethnicity retained a significant association with selected iron status markers (sTfR and body iron) and urine iodine, with NHB (but not MA) having lower iron and iodine status compared to NHW; 2) smoking and alcohol consumption retained significant positive associations with iron status; and 3) supplement use and age retained significant positive associations with urine iodine.

#### Iron status

As the correlations between the iron status biomarkers and the sociodemographic and lifestyle variables were weak or not significant, it was not surprising that each individual variable explained 5% of the variability in biomarker concentrations in bivariate analyses, and that all variables together in a multiple regression model only explained between 4–13% of the biomarker variability. Other studies on determinants of iron status found similar  $R^2$  estimates of <20% (33–34). Three variables—race-ethnicity, smoking, and alcohol consumption—emerged in the adjusted model as moderately strong and consistent correlates of iron status biomarkers.

Previous NHANES analyses of US women also found an association between iron deficiency (assessed by the ferritin or body iron model), FER or sTfR concentrations and race-ethnicity, with lower iron status in NHB compared to NHW women (6–9). Race-ethnic differentials in iron status may be related to dietary iron intake. Kant *et al.* showed that in NHANES III iron intake was lower in NHB (11.7 mg) compared to NHW (13.1 mg) women, but was similar in MA (12.5 mg) and NHW women (6). However, the observed association between FER and ethnicity remained unchanged after the authors added 24-h iron intake to their regression model. FER is an indicator of storage iron and may not reflect dietary intake; the absolute amount of dietary iron is less important than the kind of iron and type of meal in which it is found, because of large differences in heme and nonheme iron bioavailability, absorption, and influence of other dietary components (vitamin C and meat enhance, while phytate, fiber, and polyphenols inhibit the absorption of nonheme iron) (35). Consumption of heme iron has been shown to be a major and positive dietary determinant of iron stores (33,36), but nearly half of iron consumed by the US population is from grain products (nonheme) and only about one fifth is from meat, fish, and poultry (heme) (37).

Regular consumption of alcohol is known to disrupt normal iron metabolism, resulting in the excess deposition of iron in the liver in one-third of alcoholic subjects (38). A positive dose-response relationship between the amount of alcohol consumed and FER concentrations has also been observed in the general population (33,34,39,40), suggesting that the effect of alcohol on iron metabolism may start at a lower level of consumption than was previously believed. We found not only a positive association of alcohol consumption (1 drink/d) with

FER (21% higher), but also with body iron (~1 mg/kg higher) and a negative association with sTfR (6% lower).

Smoking status has not been clearly established as a determinant of FER concentrations (41,42). A recent study reported that sTfR concentrations in young Belgian women were ~9% lower in current smokers (33), which corresponded well with our finding of 10% lower estimated sTfR concentrations in women who smoked. As we saw with alcohol consumption, smoking was also associated with each iron status indicator (FER 24% and body iron ~1 mg/kg higher). It is not known to what extent dietary habits of smokers may contribute to this. Smokers are known to have higher meat intake and saturated fat consumption (43,44), indicators of more heme iron. Smoking may also have an independent effect on iron metabolism, unrelated to dietary intake.

A 25% increase in BMI in our study was associated with slightly higher estimated FER (7%) and sTfR (6%) concentrations, which is consistent with findings from NHANES III, where FER and C-reactive protein in adults progressively increased with BMI, while serum iron and transferrin saturation progressively decreased (45). Data from the Mexican Nutrition Survey also showed that obese compared to normal-weight women had a higher prevalence of ID (as measured by serum iron and transferrin saturation) despite similar dietary iron intakes in the two groups (46). An observational study in obese and nonobese adults found that the obesity-related hypoferremia (low serum iron) was not explained by differences in reported intake of heme and nonheme iron or intake of dietary variables that can affect iron absorption (47). Instead, the effect of obesity on iron status seems to parallel that of anemia of chronic disease, but without the anemia (45).

#### **lodine status**

As seen with iron status indicators, the correlations between urine iodine and the sociodemographic and lifestyle variables were weak and in some cases not significant. It was not surprising to find a moderate and significant correlation between uCr and urine iodine, as creatinine has an established relationship with urine biomarker measurements and is generally used to adjust concentrations of urine analytes for variations in hydration status. However, because uCr concentrations differ greatly among different demographic groups, it has been suggested that for multiple regression analysis of population groups, the analyte concentration (unadjusted for uCr) be included in the model with uCr added as a separate independent variable (48). To allow separate interpretation of the effect of uCr on urine iodine, we evaluated each variable in a fourth model that adjusted for uCr in addition to the 10 sociodemographic and lifestyle variables. In this model, 41% of the variability of urine iodine concentrations was explained, a much larger proportion than with model 3 (7%).

Three variables—race-ethnicity (NHB vs. NHW), supplement use, and age—emerged in the full regression model as correlates of iodine status. Race-ethnic and age differences in urine iodine concentrations have been reported previously throughout NHANES (15–18), however this is to our knowledge the first analysis that showed an association after adjusting for selected sociodemographic and lifestyle variables. We observed estimated urine iodine concentrations to be 11% higher for every 10 y increase in age. The lower urine iodine concentrations seen in NHB compared to NHW may be explained by the high prevalence

rate (70–75%) of lactase insufficiency and consequent lactose maldigestion among African-Americans (49), which likely leads to self-imposed dietary restriction of milk and milk products. Dairy products are an important contributor to iodine status among women in the United States (14), as well as other populations (50,51). In the United States, NHB have the lowest and NHW the highest per capita intake of calcium, a proxy for consumption of milk and milk products (52).

We found higher urine iodine concentrations in supplement users vs. nonusers in each model (22% in model 4 vs. 14% in model 1). Gregory *et al.* showed that among reproductive age women in the United States, a much smaller percentage report consumption of supplements with iodine (20%) compared to any supplement (43%) (19). The crude measure of *any* supplement used in our analysis may be an indicator of generally healthy behavior, possibly giving preference to iodized salt.

Adult sex differences in iodine status are not well studied because most surveys are limited to children and/or women of reproductive age. Previous analyses of NHANES data showed that females had lower urine iodine concentrations compared to males (15–18). We also observed this sex differential in models 1 to 3. However, after we also included uCr into the model, the sex difference disappeared, possibly owing to the fact that men have higher muscle mass and therefore higher uCr concentrations (48). Other variables assessed in this analysis had weak or no association with urine iodine concentrations. We observed a negative association for alcohol consumption, however the estimated change in urine iodine concentrations was small (7%).

# Summary

To our knowledge, this is the first study that examined the association of demographic, socioeconomic, and lifestyle variables on iron and iodine biomarkers available in the more recent continuous NHANES. We applied a systematic modeling approach and limited data driven decisions in the model building process to preserve the statistical properties of *P*-values and coefficients (32). Additionally, our hierarchical chunk regression modeling provided a natural way to systematically assess the magnitude of an estimated change in biomarker concentration with change in a covariate, holding all other variables constant, across biomarkers. This systematic approach allowed us to assess the relative importance of 10 sociodemographic and lifestyle variables across biomarkers in this paper and across other classes of nutritional indicators in other papers in this journal supplement (a summary table is presented in [32]). Associations of our study variables with the new indicator body iron are of particular interest because this indicator allows the evaluation of the full range of iron status of populations and is less affected by inflammation than FER (4).

Our analysis is not without limitations. Because of the cross-sectional nature of NHANES, we cannot draw any causal relationships between the biomarkers and variables. Our results could be confounded by unmeasured biological and genetic variables. In a separate analysis we investigated whether fasting or time of specimen collection as preanalytical variables and inflammation, kidney function, or pregnancy as physiological variables are associated with these biomarkers (53). Because of a limited number of degrees of freedom, we did not test for interactions between variables, between nutrients (e.g., iron and vitamin C), or between

variables and nutrients. Whether certain health conditions or health risk factors are associated with iron or iodine biomarkers was outside the scope of this investigation and so was the question whether dietary intake or intake of specific dietary supplements are associated with these biomarkers or interact with variables included in our analysis. While dietary intake of iron and iodine is known to be a major determinant of biomarkers, iron status indicators are only weakly correlated to recent dietary intake of total iron (35) and information on dietary intake of iodine is not readily available in NHANES 2003–2006. Furthermore, both intake and biomarkers are indicators of nutritional status. We chose to describe how biomarkers were associated with certain variables after adjusting for sociodemographic and lifestyle variables and within that scheme dietary intake was more naturally an outcome variable than a covariate. Nonetheless, we cannot answer the question whether the associations in our descriptive analysis are explained by intake or not. In summary, we conclude that in this adult population (women only for iron biomarkers) raceethnicity (NHB vs. NHW) was the only common variable that was associated with both iron and iodine biomarkers after adjusting for sociodemographic and lifestyle variables. Furthermore, iron biomarkers were associated with smoking and alcohol consumption, while urine iodine was associated with supplement use and age. This analysis provides a foundation for researchers that attempt to build predictive models to help answer specific hypotheses in the area of nutrition and health.

# **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Spearman correlation coefficients describing bivariate associations between each iron and iodine status biomarker and selected continuous sociodemographic and lifestyle variables for adults 20 y, NHANES 2003–2006 *J.2.3* 

	Wome	Adults 20 y of age		
Variable	Serum ferritin	Serum sTfR	Body iron	Urine iodine
Age	0.11*	0.03	0.14*	0.12*
PIR	0.06*	-0.09*	0.03	-0.03
Smoking	0.05	-0.06	0.07*	-0.03
Alcohol consumption <sup>4</sup>	0.07	-0.16*	0.09*	-0.03
BMI	0.06*	0.24*	0.01	0.10*
Physical activity <sup>5</sup>	0.00	-0.02	-0.02	0.06*
Urine creatinine 6	n/a	n/a	n/a	0.52*

Data for iodine only available for a 1/3 subsample

 $<sup>^2</sup>_{\rm sTfR}$  , soluble transferrin receptor; PIR, family poverty income ratio

<sup>&</sup>lt;sup>3</sup>Sample sizes for each biomarker by variable can be found in Supplemental Table 2; the total *n* for each biomarker was: 2539 (ferritin), 2513 (sTfR), 2509 (body iron), and 3066 (urine iodine)

 $<sup>{\</sup>small 4} \\ {\small Alcohol \ consumption: calculated \ as \ average \ daily \ consumption \ [(quantity \times frequency)/365.25]; \ 1 \ drink} \approx 15 \ g \ ethanol \ (quantity \times frequency)/365.25]; \ 1 \ drink$ 

 $<sup>{}^{5}</sup>_{\text{Physical activity: calculated as total metabolic equivalent task (MET)-min/wk from self-reported leisure time physical activities}$ 

 $<sup>^{6}</sup>$ Correlation between urine iodine and urine creatinine was assessed because the concentration of urine-based analytes is often expressed per gram creatinine to correct for the urine dilution

Significant correlation; P < 0.05

Table 2 Unadjusted iron and iodine status biomarker concentrations by sociodemographic variable categories for adults 20 y, NHANES  $2003-2006^{1,2,3}$ 

	Women 20-49 y of age			Adults 20 y of age
Variable	Serum ferritin	Serum sTfR	Body iron	Urine iodine
	$\mu g/L$	mg/L	mg/kg	$\mu g/L$
Age, y				
20-39	38.1 (36.1 – 40.2)	3.42 (3.36 – 3.49)	5.51 (5.29 – 5.73)	135 (126 – 144)
40–49	43.2 (39.0 – 47.7)	3.52 (3.38 – 3.65)	5.88 (5.46 – 6.30)	n/a
40–59	n/a	n/a	n/a	137 (128 – 147)
60	No data	No data	No data	187 (170 – 205)
P-value <sup>4</sup>	0.05	0.17	0.06	<0.0001
r <sup>2</sup> , % <sup>5</sup>	<1	<1	<1	2
Sex				
Men	No data	No data	No data	162 (152 – 173)
Women	39.9 (38.2 – 41.7)	3.46 (3.39 – 3.53)	5.65 (5.47 – 5.83)	133 (126 – 140)
P-value	n/a	n/a	n/a	<0.0001
r <sup>2</sup> , %	n/a	n/a	n/a	1
Race-ethnicity $^6$				
MA	33.5 (29.0 – 38.8)	3.46 (3.33 – 3.59)	5.02 (4.41 – 5.64)	164 (152 – 176)
NHB	35.8 (32.9 – 38.9)	4.21 (4.09 – 4.33)	4.60 (4.27 – 4.92)	133 (122 – 145)
NHW	42.0 (39.6 – 44.7)	3.33 (3.23 – 3.43)	5.96 (5.69 – 6.23)	150 (143 – 157)
P-value	0.0040	<0.0001	0.0496	<0.0001
r <sup>2</sup> , %	1	5	2	1
Education				
<high school<="" td=""><td>38.0 (32.8 – 44.0)</td><td>3.53 (3.40 – 3.67)</td><td>5.40 (4.80 – 6.01)</td><td>156 (143 – 170)</td></high>	38.0 (32.8 – 44.0)	3.53 (3.40 – 3.67)	5.40 (4.80 – 6.01)	156 (143 – 170)
High school	38.4 (35.8 – 41.3)	3.44 (3.34 – 3.54)	5.51 (5.20 – 5.81)	156 (144 – 169)
>High school	41.0 (38.8 – 43.3)	3.44 (3.37 – 3.52)	5.76 (5.54 – 5.98)	139 (130 – 148)
P-value	0.19	0.35	0.45	0.0252
<i>1</i> <sup>2</sup> , %	<1	<1	<1	<1
PIR <sup>7</sup>				
Low	36.5 (34.5 – 38.5)	3.62 (3.52 – 3.73)	5.16 (4.90 – 5.41)	148 (138 – 158)
Medium	39.6 (36.0 – 43.5)	3.48 (3.36 – 3.59)	5.59 (5.19 – 5.99)	159 (148 – 170)
High	42.4 (39.4 – 45.5)	3.34 (3.26 – 3.42)	5.98 (5.71 – 6.26)	138 (129 – 148)
P-value	0.0056	<0.0001	0.42	0.0160
r <sup>2</sup> , %	<1	1	1	<1

<sup>&</sup>lt;sup>1</sup>Biomarker concentrations represent geometric means (arithmetic mean for body iron) and 95% CI; sTfR, soluble transferrin receptor; SI conversion factors are as follows: FER, ×2.247 (pmol/L); sTfR (no generally accepted conversion variable available); urine iodine, ×7.88 (nmol/L)

Data for iodine only available for a 1/3 subsample

<sup>&</sup>lt;sup>3</sup>Sample sizes for each biomarker by variable can be found in Supplemental Table 2; the total *n* for each biomarker was: 2539 (ferritin), 2513 (sTfR), 2509 (body iron), and 3066 (urine iodine)

 $^4P$  value based on Wald F test, which tests whether at least one of the means across the categories is significantly different

 $<sup>^{5}</sup>$ r<sup>2</sup> based on model 1, simple linear regression, using categories as shown

 $<sup>^{6}{\</sup>rm MA},$  Mexican American; NHB, non-Hispanic black; NHW, non-Hispanic white

<sup>7</sup> PIR, family poverty income ratio: 0–1.85 (low); >1.85–3.5 (medium); >3.5 (high)

Pfeiffer et al.

Table 3 Unadjusted iron and iodine status biomarker concentrations by lifestyle variable categories for adults 20 y, NHANES  $2003-2006^{1,2,3}$ 

Women 20-49 y of age				Adults 20 y of age
Variable	Serum ferritin	Serum sTfR	Body iron	Urine iodine
	$\mu g/L$	mg/L	mg/kg	$\mu g/L$
Supplement use <sup>4</sup>				
No	42.1 (39.3 – 45.0)	3.40 (3.33 – 3.47)	5.90 (5.62 – 6.17)	155 (147 – 163)
Yes	37.7 (35.2 – 40.4)	3.51 (3.39 – 3.64)	5.38 (5.06 – 5.70)	136 (127 – 145)
P-value <sup>5</sup>	0.0491	0.11	0.14	0.0006
<sub>1</sub> <sup>2</sup> ,% 6	<1	<1	<1	1
Smoking <sup>7</sup>				
No	37.7 (35.7 – 39.7)	3.56 (3.48 – 3.64)	5.34 (5.12 – 5.57)	149 (141 – 158)
Yes	46.7 (42.6 – 51.2)	3.20 (3.08 – 3.32)	6.47 (6.07 – 6.88)	138 (129 – 148)
P-value	0.0005	< 0.0001	0.0003	0.08
$r^2$ ,%	1	2	2	<1
Alcohol consumpti	ion <sup>8</sup>			
No drinks	36.5 (33.4 – 39.9)	3.64 (3.52 – 3.76)	5.14 (4.77 – 5.51)	168 (155 – 182)
<1 (not 0)	40.0 (37.9 – 42.2)	3.41 (3.34 – 3.47)	5.71 (5.49 – 5.94)	140 (130 – 151)
1-<2	56.3 (47.0 – 67.3)	3.16 (2.96 – 3.36)	7.23 (6.45 – 8.00)	137 (114 – 164)
2	NR 10	NR	NR	122 (108 – 137)
P-value	<0.0001	0.001	0.0002	0.0019
r <sup>2</sup> ,%	2	2	2	1
$BMI^9$				
Underweight	43.0 (36.0 – 51.4)	3.00 (2.76 – 3.26)	6.45 (5.60 – 7.30)	NR
Normal weight	37.9 (35.4 – 40.5)	3.22 (3.14 – 3.32)	5.69 (5.39 – 5.99)	130 (120 – 140)
Overweight	38.8 (35.2 – 42.8)	3.43 (3.30 – 3.55)	5.59 (5.15 – 6.02)	153 (140 – 167)
Obese	43.0 (39.6 – 46.6)	3.80 (3.68 – 3.92)	5.59 (5.23 – 5.95)	156 (146 – 167)
P-value	0.10	< 0.0001	0.0312	<0.0001
r <sup>2</sup> ,%	<1	5	<1	1
Physical activity 11	!			
No activity	36.9 (34.1 – 40.0)	3.56 (3.42 – 3.71)	5.27 (4.88 – 5.66)	160 (149 – 171)
0-<500	41.3 (37.2 – 45.9)	3.48 (3.37 – 3.59)	5.75 (5.33 – 6.16)	134 (124 – 146)
500-<1000	38.5 (34.5 – 43.0)	3.37 (3.21 – 3.53)	5.61 (5.13 – 6.09)	142 (124 – 162)
1000	42.0 (39.1 – 45.1)	3.38 (3.29 – 3.47)	5.90 (5.59 – 6.20)	144 (132 – 156)
P-value	0.14	0.14	0.69	0.0082
$r^2$ ,%	<1	<1	<1	1

<sup>1</sup> Biomarker concentrations represent geometric means (arithmetic mean for body iron) and 95% CI; sTfR, soluble transferrin receptor; SI conversion factors are as follows: FER, ×2.247 (pmol/L); sTfR (no generally accepted conversion variable available); urine iodine, ×7.88 (nmol/L)

<sup>&</sup>lt;sup>2</sup>Data for iodine only available for a 1/3 subsample

 $^{3}$ Sample sizes for each biomarker by variable can be found in Supplemental Table 2; the total n for each biomarker was: 2539 (ferritin), 2513 (sTfR), 2509 (body iron), and 3066 (urine iodine)

- $^{4}\mbox{``Supplement user''}$  defined as participant who reported taking a dietary supplement within the past 30 d
- $^{5}P$ -value based on Wald F test, which tests whether at least one of the means across the categories is significantly different
- $^{6}r^{2}$  based on model 1, simple linear regression, using categories as shown
- $^{7}\mbox{``Smoker''}$  defined by serum cotinine concentration >10  $\mu\mbox{g/L}$
- ${}^{8}\text{Alcohol consumption: calculated as average daily consumption [(quantity \times frequency)/365.25]; 1 drink} \approx 15 \text{ g ethanol consumption}$
- $^9$ BMI (kg/m $^2$ ) definitions: <18.5(underweight); 18.5–<25 (normal weight); 25–<30 (overweight); and 30 (obese)
- 10 Estimate not reported due to small sample size (n<42)
- <sup>11</sup>Physical activity: calculated as total metabolic equivalent task (MET)-min/wk from self-reported leisure time physical activities

**Table 4**Estimated change in biomarker concentrations of iron and iodine status after adjusting for sociodemographic and lifestyle variables through chunk-wise modeling using data for adults 20 y, NHANES 2003–2006 1,2,3

	Wom	Adults 20 y of age Urine iodine		
Variable	Serum ferritin Serum sTfR Body iron			
Age: every 10 y increase				
Model 1	12.6*	1.2	0.4*	7.8*
Model 2	10.4*	2.4*	0.3*	8.0*
Model 3	7.6*	1.5	0.2*	6.3*
Model 4	n/a	n/a	n/a	11.4*
Sex: women vs. men				
Model 1	n/a	n/a	n/a	-18.2*
Model 2	n/a	n/a	n/a	-19.2*
Model 3	n/a	n/a	n/a	-25.5*
Model 4	n/a	n/a	n/a	3.8
Race-ethnicity 4: NHB vs. N	HW			
Model 1	-14.8*	26.5*	-1.4*	-11.3*
Model 2	-11.9*	24.8*	-1.2*	-11.7*
Model 3	-6.6	18.8*	-0.8*	-12.0*
Model 4	n/a	n/a	n/a	-33.7*
Race-ethnicity 4: MA vs. NF	НW			
Model 1	-20.2*	3.9	-0.9*	9.3*
Model 2	-15.3*	2.5	-0.7	8.1
Model 3	-3.9	-3.9	0.0	6.4
Model 4	n/a	n/a	n/a	3.7
Education <sup>5</sup> : HS vs. >HS				
Model 1	-6.7	0.8	-0.3	12.7*
Model 2	-1.8	-2.7	0.0	7.1
Model 3	-5.0	-2.6	-0.1	7.4
Model 4	n/a	n/a	n/a	4.6
PIR <sup>6</sup> : every 2 unit decrease				
Model 1	-8.1*	4.7*	-0.5*	4.5
Model 2	-3.4	3.9*	-0.3	5.6*
Model 3	-4.2	3.4*	-0.3*	8.4*
Model 4	n/a	n/a	n/a	3.4
Supplement use <sup>7</sup> : yes vs. no	)			
Model 1	11.5*	-3.1	0.5*	14.2*
Model 3	6.0	-1.1	0.3	18.8*

	Women 20–49 y of age			Adults 20 y of age	
Variable	Serum ferritin	Serum sTfR	Body iron	Urine iodine	
Model 4	n/a	n/a	n/a	22.1*	
Smoking 8: yes vs. no					
Model 1	24.0*	-10.1*	1.1*	-7.4	
Model 3	24.2*	-10.7*	1.1*	-1.0	
Model 4	n/a	n/a	n/a	-6.6	
Alcohol consumption 9: 1 vs. 0 drinks/d					
Model 1	28.8*	-10.9*	1.3*	-10.4*	
Model 3	21.3*	-5.9 *	0.9*	-11.6*	
Model 4	n/a	n/a	n/a	-7.1 *	
BMI 10: 25% increase					
Model 1	5.7*	7.5*	-0.0	9.5*	
Model 3	7.2*	6.0*	0.0	7.4*	
Model 4	n/a	n/a	n/a	-0.5	
Physical activity $^{II}$ : 750 vs. 150 MET-min/wk					
Model 1	2.2*	-1.1*	0.1*	-2.2*	
Model 3	2.9*	-0.7	0.1	-0.5	
Model 4	n/a	n/a	n/a	0.1	

<sup>&</sup>lt;sup>1</sup>Change represents percent change (%) in geometric mean for all biomarkers except for body iron where change in arithmetic mean represents units (mg/kg); sTfR, soluble transferrin receptor

<sup>&</sup>lt;sup>2</sup>Model 1, simple linear regression; model 2, multiple linear regression by adjusting for sociodemographic variables; model 3, multiple linear regression by adjusting for sociodemographic and lifestyle variables; change in covariate was carried out while holding any other variables in the model constant

<sup>&</sup>lt;sup>3</sup>Sample sizes for each biomarker by variable can be found in Supplemental Table 2 (model 1) and Supplemental Table 4 (models 2–4); the total *n* for each biomarker was: 2539 (ferritin), 2513 (sTfR), 2509 (body iron), and 3066 (urine iodine)

<sup>&</sup>lt;sup>4</sup>MA, Mexican American; NHB, non-Hispanic black; NHW, non-Hispanic white

<sup>&</sup>lt;sup>5</sup>HS, high school

PIR, family poverty income ratio

 $<sup>^{7}</sup>$  "Supplement user" defined as participant who reported taking a dietary supplement within the past 30 d

 $<sup>^8</sup>$ "Smoker" defined by serum cotinine concentration >10  $\mu$ g/L

<sup>9</sup> Alcohol consumption: calculated as average daily consumption [(quantity  $\times$  frequency)/365.25]; 1 drink  $\approx$  15 g ethanol

<sup>10</sup> A 25% increase in BMI is comparable to a change from being normal weight to overweight

<sup>&</sup>lt;sup>11</sup>Physical activity: calculated as total metabolic equivalent task (MET)-min/wk from self-reported leisure time physical activities

<sup>\*</sup> Change is significantly different from zero; *P*<0.05